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Utility of blood cultures in community-acquired pneumonia requiring hospitalization: influence of antibiotic treatment before admission

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It has been previously shown that antibiotics given before hospitalization significantly reduce the proportion of positive blood cultures in community-acquired pneumonia (CAP). The aim of this prospective study was to compare the utility and cost-benefits of blood cultures in patients, hospitalized for moderate CAP, who had or had not received antibiotic therapy prior to admission.

During 1 year, 53 patients were included and separated into two groups: group 1 patients had not received antibiotic treatment prior to admission ($n=30$), whereas group 2 patients had been treated with antibiotics ($n=23$). Within the first 48 hours, a set of blood cultures was collected if the body temperature was higher than 38·5°C or in the case of shaking chills.

A total of 136 blood cultures was collected; 74 in group 1 and 62 in group 2. Bacteraemia was significantly more frequent in group 1 than in group 2, 5/30 patients *vs.* 0/23, respectively ($P<0·05$). The cost of negative blood cultures was valued at 13,939.2 FF in group 1 and 13,164.8 FF in group 2, respectively 464.6 ± 244.3 FF and 569.3 ± 233.4 FF per patient (n.s.). Moreover, blood cultures were the method of diagnosis in only one of the five patients with bacteraemia and in no case did a positive blood-culture result influence the initial therapeutic regime.

Thus, our results suggest a reduced clinical utility and cost-benefit of blood cultures in patients hospitalized for moderate CAP who have received an antibiotic treatment prior to admission.

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Introduction

In patients hospitalized for community-acquired pneumonia (CAP), bacteraemia occurs in 0·5–14% (1,2) with a low sensitivity of blood cultures in such cases. In 1993, the guidelines of the American Thoracic Society recommended that hospitalized patients with CAP should have two sets of blood cultures collected (3). However, Chalasani *et al.* have recently suggested that blood cultures may have a questionable cost-effectiveness (4). Indeed, it has been previously shown that antibiotics given before admission can significantly reduce the proportion of positive blood cultures in patients with CAP (5,6). From all these results, it would be conceivable to assume that blood cultures are of limited value especially in patients that have received an antibiotic treatment prescribed before admission. Thus, we conducted a prospective study in patients hospitalized for moderate CAP to assess the impact of such antibiotic treatment on bacteraemia. We report here a cost-benefit analysis, taking into account the relationships that we observed between blood cultures and antibiotic treatment given before hospitalization.

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Methods

PATIENTS

From 1 March 1994 to 28 February 1995, all patients over 15 years of age hospitalized in the respiratory unit of our hospital for moderate CAP were included in a prospective study. Pneumonia was defined as any acute septic episode with respiratory symptoms and a new or progressive infiltrate on chest X-rays. Community-acquired infection was defined as an infection occurring before or within 48 h after admission in patients that had not been hospitalized during the preceding 2 weeks. Moderate pneumonia corresponded to an infection requiring hospitalization in a respiratory unit but not in an intensive care unit. Patients with a clinical history suggestive of aspiration, a severe pneumonia requiring an intensive care unit, an immunosuppressive illness or

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who were being treated with immunosuppressive drugs were excluded from the study. In all patients, we looked for an antibiotic treatment prescribed before hospitalization and we recorded the type of antibiotics, the dosage and the duration of therapy.

MICROBIOLOGICAL METHODS

In each patient, a bronchial sample was taken during the 12 h following admission and before the onset of antibiotic therapy. A sputum sample was obtained when a sputum could be produced spontaneously. In the other patients, a sample was obtained via a fibre-optic bronchoscope: a bronchial aspiration or a minimal bronchial washing [instillation (50 ml) and aspiration of a physiological solution] was performed in segmental bronchi corresponding to the infiltrate on chest X-rays. After Gram staining, each bronchial sample was cultured on 5% horse's blood and chocolate agars to obtain a quantitative identification.

Within 48 h of hospital admission, blood cultures were collected (before or after the onset of hospital antibiotic treatment) only if the body temperature was higher than 38·5°C or in cases of shaking chills. Blood (10 ml per set) was injected into two culture bottles (one aerobic and the other anaerobic) that were transferred to the microbiology laboratory for incubation in a Bactec NR 660 (Becton Dickinson, MD, U.S.A.) and processing. In culture bottles giving a positive growth-index indication, Gram staining was initially performed and then two 5% horse blood agars were seeded aerobically and anaerobically. Moreover, according to the results of the Gram stain, blood specimens could be cultured on chocolate and BCP agars.

Serologies against atypical germs and viruses were obtained within 24 h of admission and 15 days later if possible. Tests for pneumococcal antigens were performed on serum and urine.

DIAGNOSTIC DEFINITIONS

The bronchial samples were considered of good quality if the Gram stain showed fewer than 10 squamous cells and more than 25 leukocytes per low-power field. The micro-organism was considered to be the aetiological agent when it was isolated from the sputum sample, bronchial aspiration or minimal bronchial washing at a level equal to or higher than 10^7, 10^6 and 10^4 colony-forming units (CFU) ml^{-1} respectively. Serological results were considered as diagnostic when there was a four-fold rise in antibody titers. *Streptococcus pneumoniae* was considered to be responsible for the infection if pneumococcal antigens were found in serum and/or urines.

Blood cultures were considered to be contaminated if they showed only coagulase-negative staphylococci, viridans streptococci, aerobic or anaerobic Gram-positive bacilli. The criteria of true bacteraemia were: two separate blood cultures growing the same micro-organism; one positive blood culture associated with a bronchial sample identifying the same germ; or one blood culture isolating a germ and the presence of at least two of the following symptoms: respiratory rate over 20 min^{-1}, pulse rate over 90 min^{-1}, temperature over 38·5°C or change in the blood leukocyte count (7).

COST OF BLOOD CULTURE

In 1995, the cost of a negative set of blood cultures was 211.2 FF. The price rose to 246.4 FF when a germ was isolated (contaminated cultures or not). When an antibiogram was performed for a positive blood culture set, the cost was 316.8 FF. When more than one blood sample grew the same germ, the antibiogram was performed on a simple set.

STATISTICAL ANALYSIS

Qualitative data from the two groups were compared using Fischer's test. Quantitative data two groups were compared using the Student's *t*-test. The results were expressed as mean ± SD. A *P*-value of $<0·05$ was considered significant.

Results

POPULATION

During 1 year, 53 patients hospitalized for CAP in our department were included in the study: 33 men and 20 women. Mean age was 55·7 ± 18 years (range 16–85 years). These patients were separated into two groups: group 1 patients had not received antibiotic treatment prior to admission ($n=30$), whereas group 2 patients had been treated with antibiotics ($n=23$). The most frequent underlying diseases were chronic obstructive pulmonary disease (COPD) (32%), congestive heart failure, and alcoholism (13·2%). There was no significative difference in frequency of co-existing illnesses between the two groups.

In group 2 patients, the duration of antibiotic treatment before hospitalization was 7·2 ± 6·5 days. The most commonly prescribed antibiotics were macrolides (nine patients), third-generation cephalosporins (six patients), first-generation cephalosporins and ampicillin/amoxycillin (five patients), and amoxycillin + clavulanate (four patients).

AETIOLOGICAL DIAGNOSIS

A sputum sample was obtained in 13 patients (24·5%), a bronchial aspiration in 19 patients (35·8%) and a minimal bronchial washing in 21 patients (39·6%). A final diagnosis was obtained in 32 patients (60·4%). The most frequently identified microbial agent was *Streptococcus pneumoniae* ($n=13$) followed by *Haemophilus influenzae* ($n=9$), and Gram-negative bacilli ($n=5$).

BLOOD CULTURES

Table 1 shows results from the 136 blood cultures collected (74 in group 1 and 62 in group 2). Bacteraemia was exclusively observed in group 1 patients (5/30 *vs.* 0/23 in

TABLE 1. Comparison of blood culture results in two groups of patients. For per patient results, values are median ± SD

	Group 1 (n=30)	Group 2 (n=23)	P-value
Blood cultures	74	62	
Blood cultures per patient	2·5 ± 1·1	2·7 ± 1·1	n.s.
Patients with bacteraemia	5	0	<0·05
Positive blood cultures	8	0	<0·01
Cost of blood cultures (FF)	16,262.4	13,164.8	
Cost of negative blood cultures (FF)	13,939.2	13,164.8	
Cost of negative blood cultures (FF) per patient	464.6 ± 244.3	569.3 ± 233.4	n.s.

group 2 patients, P<0·05). In group 1, eight blood cultures were positive in these five patients (two in three patients and one in two others) whereas in group 2, no blood culture was positive (P<0·01). The isolated microorganisms were *Streptococcus pneumoniae* and *Haemophilus influenzae* (in four and one patients, respectively). In two patients from group 2, a coagulase-negative staphylococcus was identified.

The total cost of blood cultures was 29,427.2 FF (16,262.4 FF for group 1 and 13,164.8 FF for group 2). The cost of negative blood cultures corresponds to the cost that could be saved if blood cultures were abandoned. Expressed per patient, this cost was higher in group 2 (569.3 ± 233.4 FF) than in group 1 (464.6 ± 244.3 FF), but the difference was not significant.

The effective cost of one positive blood culture that could be estimated through the ratio of total cost of blood cultures divided by the number of positive blood cultures was 2032.8 FF for group 1. In fact, to obtain a positive culture in this group, eight blood cultures were performed and were negative. This ratio could not be evaluated in group 2 as no blood culture was positive.

Furthermore, blood culture was the only microbiological method used in assessing diagnosis in only one of the five patients with bacteraemia. Finally, the micro-organisms isolated from blood cultures were always susceptible to the initial antibiotic therapy given during hospitalization and in none of these five patients did the microbiological results influence the hospital antibiotic treatment.

Discussion

This prospective study was conducted to assess the influence of antibiotic therapy given prior to admission on the results and the clinical utility of blood culture. Our results showed low cost-effectiveness of this microbiological method in patients who had received antibiotic treatment before hospitalization. Moreover, this study suggests a poor impact of the positive blood culture on prescription of the hospital antibiotic treatment.

Some aspects of this study merit consideration. The number of patients, corresponding to 1 year's admission to our respiratory unit, is small but sufficient at least to give an idea of what relevance blood culture may have in such a group; however, without allowing any definite conclusion to be drawn. Moreover, the number of blood cultures was not insignificant and the interest of this study lay in the comparison between patients who had or had not received antibiotics before admission.

Only patients with a moderate pneumonia requiring hospitalization according to the ATS guidelines were included in this study. Indeed, in severe pneumonia, blood cultures appear to be more frequently positive than in cases of moderate pneumonia. Moreover, bacteraemia is a prognostic factor associated with mortality (8–10) which shows the relevance of blood culture in severe CAP. In this study, we also excluded patients with an immunosuppressive illness or who were being treated with immunosuppressive drugs because it has been previously demonstrated that the risk of bacteraemic pneumonia is increased in these patients (11,12).

Blood cultures were collected in our patients only when their temperature was higher than 38·5°C or in cases with shaking chills, considered to be clinical predictors for true bacteraemia (13). Also, only five out of 53 patients had true positive blood cultures (9·4%). This low percentage is in agreement with the literature, which reports a frequency ranging from 0·5 to 14% in CAP (1,2,5,6,14–18). Moreover, in agreement with most studies (4,6,17), we found that *Streptococcus pneumoniae* was the most common bacteria found in bacteraemic pneumonia (four of five patients).

Our results show that antibiotic therapy prior to hospitalization significantly decreased the frequency of bacteraemia in CAP, as previously reported (6,15). This could be due to the fact that the antibiotic therapy given before admission had been effective, at least partially, against *Streptococcus pneumoniae*, the most frequent pathogen isolated in CAP (2,3,5,6,15–18,19–22). Thus, the use of antibiotic treatment prior to hospitalization can be considered a criterion for low risk of bacteraemia and this conclusion casts doubt on the utility of blood cultures in this group of patients.

Only a few papers have addressed the cost of the diagnostic procedures in CAP. In 1995, in a retrospective study

of 517 patients with CAP, Chalasani *et al.* reported $66 (376.2 FF) spent per patient for blood cultures, which had little influence on the therapeutic regimen. However, the authors were unable to specify whether there had been prior use of an antibiotic at home (4). In our study, the cost of blood culture per patient was higher; this could be explained by our calculation of cost per set of blood cultures and a higher number of sets performed per patient in our population than in the study of Chalasani *et al.* (4). Analysis of the cost of blood specimens in our two groups showed that the cost of negative blood cultures per patient was consistent, particularly in patients who had received antibiotic therapy prior to admission, showing the influence of this treatment on the cost-benefits of blood culture.

However, blood culture can enable a specific diagnosis with a lower probability of false-positive cultures than with bronchial samples. Indeed, even if a high minimal count of CFU per millilitre was retained, positive culture results from bronchial samples were not unequivocal. Moreover, in some centres, particularly on geriatric wards, sputum specimens or bronchial samples are rarely obtained and the aetiological diagnosis can only be acquired from blood cultures. Finally, a positive blood culture result may save money by enabling a less broad-spectrum antibiotic treatment. However, because of the absence of positive cultures in group 2, we did not analyse the additional costs of antibiotics or other treatments.

Thus, despite the small numbers, our data confirm the reduced clinical usefulness and extremely low cost-benefit of blood cultures in patients hospitalized for moderate CAP and treated with antibiotics before admission. Blood cultures are useful in microbiological specific diagnosis and decision-making in antibiotic treatment, particularly in centres where bronchial samples cannot be obtained. However, at a time when medical economy is major consideration, it can be suggested that the use of blood culture could be abandoned without deleterious consequences in those patients who have received antibiotic therapy prior to hospitalization.

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